REMARKS

Reconsideration and withdrawal of the objections and rejections of the application are requested.

I. STATUS OF CLAIMS AND FORMAL MATTERS

Claims 11, 16-18, 20-22 and 30 are pending in this application. Claims 11, 16-18 and 20-22 are amended; claim 30 is added. Support for the amended claims is found throughout the specification. No new matter is added by this amendment.

It is submitted that the claims, herewith and as originally presented, are patentably distinct over the prior art, and that these claims are in full compliance with the requirements of 35 U.S.C. §112. The amendments of and additions to the claims, as presented herein, are not made for purposes of patentability within the meaning of 35 U.S.C. §101, §102, §103 or §112 and are not narrowing amendments. Rather, these amendments and additions are made simply for clarification and to round out the scope of protection to which Applicants are entitled. Furthermore, it is explicitly stated that the herewith amendments should not give rise to any estoppel, as the herewith amendments are not narrowing amendments.

Specification

The specification was objected to because the cross-reference information was not updated to reflect issuance of the parent. The updated cross-reference information is now included.

Clarification was requested with respect to page 48 of the application. An inadvertent page break resulted in there being only one sentence on page 48. A period has been added to the end of the sentence on page 48, and no information is missing from the application.

The specification was also objected to because it did not incorporate suggested headings, such as FIELD OF INVENTION, BACKGROUND OF INVENTION, etc. While it is noted by Applicants that these are suggestions only, and **not** requirements, the specification has been amended accordingly.

Sequence Rules

The specification was objected to as not conforming to the requirements of 37 CFR 1.821. The application has been amended to insert sequence identifiers, obviating the objection.

II. THE REJECTIONS UNDER 35 U.S.C. §112, 1ST PARAGRAPH ARE OVERCOME

Claims 9-12, 16-18, 20-22 and 24 were rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking adequate written description. The rejection is traversed.

The Office Action alleges that "[t]he claims encompass a genus of unspecified components from an equine lentivirus and/or a genus of retroviral vectors derived from a non-primate lentivirus genome. The Examiner is thanked for indicating that there is sufficient written description for non-primate lentiviral vectors and/or particles obtained from the genome of various non-primate lentiviruses. New, independent claim 30 has been added, and is limited to non-primate lentiviral-based systems. Claim 30 also specifies the components of the claimed retroviral vector production system. Therefore, it is believed that written description for the invention, as claimed, is present in the application.

Claims 9-12, 16-18, 20-22 and 24 were rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking enablement. The rejection is traversed.

The Examiner is thanked for indicating the many enabled embodiments of the invention. The current claims are directed to a non-primate lentivirus-based retroviral vector production system comprising a non-primate lentivirus genome, and nucleic acid sequences encoding gag, pol, and an envelope protein, but lacking sequences encoding functional Tat. One of ordinary skill in the art would face no undue experimentation in practicing the claimed invention, in view of the disclosure in the specification and his own knowledge of the art.

Reconsideration and withdrawal of the rejections under 35 U.S.C. §112, first paragraph, are requested.

III. THE REJECTIONS UNDER 35 U.S.C. §112, 2ND PARAGRAPH, ARE OVERCOME

Claims 1-8, 10-14 and 16-29 were rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite. It is assumed that the recitation of these claims was a typographical error, and that the rejection was intended for claims 9-13, 16-18, 20-22 and 24.

Claim 9 has been cancelled, and claim 30 does not recite "derived from", obviating the rejection on that basis. Likewise, claim 12 has been cancelled, and no other pending claims recite "substantially derived from".

Claims 16 and 17 have been amended to clarify that the retroviral particle comprises a retroviral vector obtained from the vector production system of claim 30, overcoming the

rejection of claims 16 and 17.

Reconsideration and withdrawal of the rejections under 35 U.S.C. §112, second paragraph, are requested.

IV. THE ART REJECTIONS ARE OVERCOME

Claims 9-13, 16-18, 20-22 and 24 were rejected under 35 U.S.C. §102(e) as allegedly being anticipated by Olsen. The rejection is traversed.

Olsen relates to the use of an EIAV system employing all accessory genes. As is accurately stated in the Office Action, Olsen teaches that these genes reside on the packaging vector (first vector) of the system, as opposed to on the genomic vector. Olsen fails to teach or suggest the removal of any accessory genes from the system, nor does it provide motivation to remove any accessory genes from the system. In particular there is no teaching, suggestion, or motivation for making the accessory gene, *tat*, nonfunctional in the system. Thus, Olsen cannot anticipate the claimed invention.

Claims 16-18, 20-22 and 24 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Olsen taken with Naldini *et al.* and Chang. The rejection is traversed.

Olsen is discussed above. The deficiencies of Olsen are not overcome by the teachings of either Naldini or Chang, when taken alone or in combination, and in particular, when taken in the context of making a non-primate system including sequences encoding nonfunctional Tat.

With respect to the deletion or mutation of the *tat* sequence such that Tat is nonfunctional in the system, Naldini relies on the statement that 'techniques in the prior art' can be used to make Tat nonfunctional. It is noted that the Office Action relies on column 7, lines 20-30, of Naldini, which states that the "artisan can practice known techniques to render the tat gene non-functional." In fact, Naldini fails to describe the construction of a vector including sequences encoding a nonfunctional Tat. Rather, Naldini relies on an HIV vector system taught in Zufferey *et al.* (Nat. Biotech. (1997) 15:871-875), which system includes a sequence encoding functional Tat.

Quite to the contrary, the *tat* gene was considered essential for viral replication in HIV production systems at that time, and it was not until January 1998 that HIV *tat* gene mutations were described and made available in the public domain, in the context of a lentiviral vector system with nonfunctional Tat. This work was described in Kim *et al.* (J. Virol. (1998) 72:811-816), which has been made of record in this application.

Chang relates to an HIV system that requires Tat for efficient HIV-1 vector production. While Chang constructs genomic vectors that are *tat* minus (col. 28-29), these vectors are not capable of supporting efficient vector production in a lentiviral vector system. (See Example 12 of Chang.) In fact, the teachings of Chang support Applicants' view that the Naldini does not enable nonfunctional Tat in a lentiviral vector system by relying on known techniques.

In addition, there are no teachings, suggestions or otherwise in either Naldini or Chang that allow the skilled artisan to extend the concept of making HIV Tat nonfunctional to the concept of making non-primate lentiviral Tat nonfunctional. This is because neither Naldini nor Chang teach the key differences in the genomic structure of the viruses. For example, the *tat* gene in EIAV is arranged quite differently, as compared to its arrangement in the HIV virus. In EIAV, the first exon of the *tat* gene is just at the 5' end of the viral genome, before the first splice donor, which places the exon in all of the viral messages. The second exon is located among viral genes that are not present in HIV. In particular, EIAV includes the S2 gene just downstream of this second exon of *tat*, and also includes a dUTPase domain (conserved in all non-primate lentiviruses, but not present in primate lentiviruses) in the *pol* gene, upstream from this second exon of *tat*. Furthermore, the HIV *tat* gene is located among viral genes not present in EIAV or other non-primate lentiviruses, *i.e.*, accessory genes *vif*, *vpr*, *vpu*, and *nef*. The mere fact that EIAV encodes fewer accessory proteins than HIV could have meant that EIAV relied on host cell functions to complement an accessory function encoded by viral genes in the HIV system. To this end, the mere absence of functional Tat in an EIAV system would have been fraught with a high degree of unpredictability. As such, at the time of the invention, the skilled artisan would not have expected that manipulations to the *tat* gene described with respect to HIV could have been extrapolated to non-primate lentiviruses with a reasonable expectation of success. Thus, the invention is not obvious over Olsen, in combination with Naldini and Chang.

Claims 9-12, 16-18, 20-22 and 24 were rejected under 35 U.S.C. §102(e) as allegedly being anticipated by Kingsman ("the '682 patent"). The rejection is traversed.

Contrary to the statements in the Office Action, this is not a proper 102(e) reference, as the inventive entities are not "another" as to each other. The inventors of the '682 patent are Alan Kingsman, Susan Kingsman, Narry Kim, and Kyriacos Mitrophanous, while the inventors of the instant application are Alan Kingsman, Miles Carroll, Jonathan Rohll, Kyriacos Mirophanous and Narry Kim. In addition to the significant overlap of the inventors, the '682

patent and the current application were commonly owned by Oxford BioMedica ("OBM") at the time both inventions were made. The '682 patent is owned by OBM by virtue of an assignment that was recorded with the U.S. Patent Office on December 28, 1998, at reel 9676, frame 0060. The present application is owned by OBM by virtue of the assignment of U.S. application Serial No. 09/238,356, now U.S. Patent No. 6,312,683, of which this application is a divisional, recorded at reel 9892, frame 0215, on April 12, 1999.

Reconsideration and withdrawal of the rejections under 35 U.S.C. §§102 and 103 are requested.

V. THE DOUBLE PATENTING REJECTION IS OVERCOME

Claims 9-12, 16-18, 20-22 and 24 were rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-62 of U.S. Patent No. 6,521,457 in view of Olsen. Since U.S. Patent No. 6,521,457 is Olsen, and since the current application does not share common inventors or a common assignee with Olsen, it is submitted that this rejection has been made in error. Consequently, reconsideration and withdrawal are requested.

CONCLUSION

As it is believed that this application is in condition for allowance an early notice to that effect is earnestly solicited. If, however, there remains any issue outstanding, the Examiner is invited to contact the undersigned for its prompt attention.

Respectfully submitted,

FROMMER LAWRENCE & HAUG LLP
Attorneys for Applicants

By: Anne-Marie C. Yvon

Thomas J. Kowalski
Reg. No. 32,147

Anne-Marie C. Yvon, Ph.D.
Reg. No. 52,390
(212) 588-0800